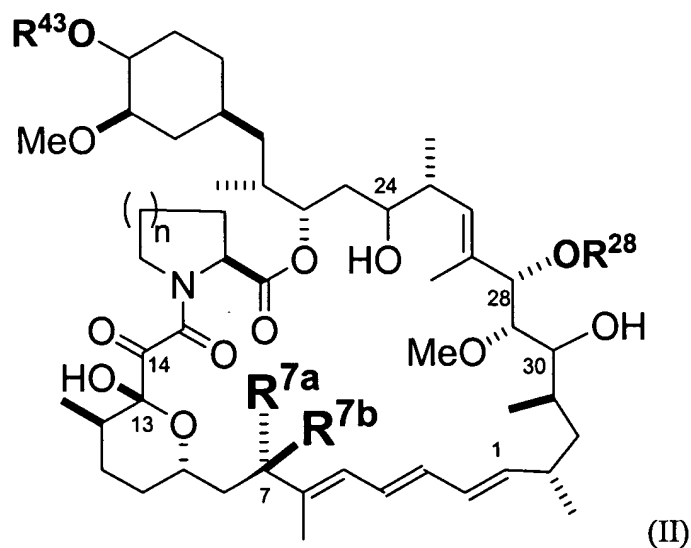
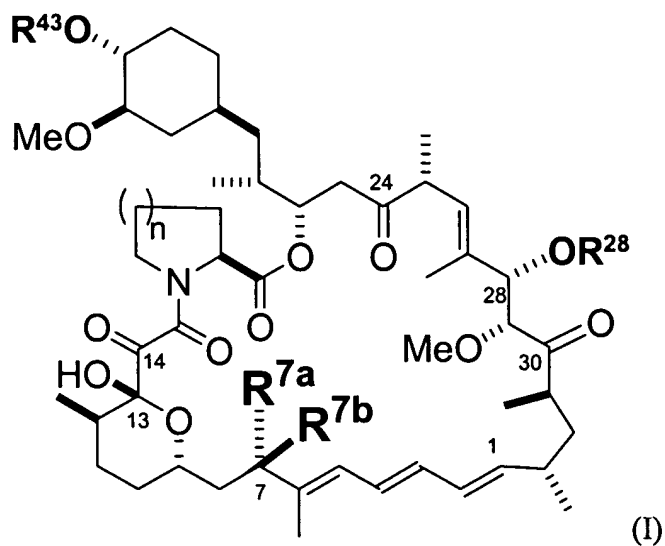


AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently amended) A compound of the formula I or II:

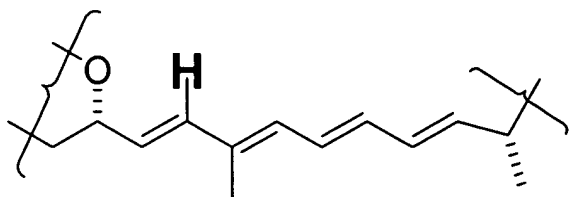


wherein

n is 1 or 2;

R^{28} and R^{43} are independently selected from the group consisting of H and an aliphatic; or acyl; ~~areyl or heteroareyl~~ moiety;

one of R^{7a} and R^{7b} is H and the other is halo, $-R^A$, $-OR^A$, $-SR^A$, $-OC(O)R^A$, $-OC(O)NR^A R^B$, $-NR^A R^B$, $-NR^B C(O)R^A$, $-NR^B C(O)OR^A$, $-NR^B SO_2 R^A$, $-NR^B SO_2 NR^A R^{B'}$ or $-NR^B C(O)NR^A R^{B'}$; or R^{7a} and R^{7b} taken together, are H in the tetraene moiety:



where R^A is H or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where R^B is H, OH or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where each aliphatic moiety is an independently chosen saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms;

where each heteroaliphatic moiety is an independently chosen 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;

where each aryl moiety is an independently chosen 6-14-membered mono- or polycyclic unsaturated moiety;

where each heteroaryl moiety is an independently chosen 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms; and

where each acyl moiety is an independently chosen $-OCR$ group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;
or a pharmaceutically acceptable salt thereof.

2. **(Previously presented)** The compound of claim 1, 78 or 79 wherein n is 2, R^{28} is H, R^{7a} is -OMe, R^{7b} is H and R^{43} is an aliphatic moiety.

3. **(Previously presented)** The compound of claim 1, 78 or 79 wherein R^{7a} is -OMe and R^{7b} is H.

4. **(Previously presented)** The compound of claim 1, 78 or 79 wherein R^{28} is H.
5. **(Previously presented)** The compound of claim 1, 78 or 79 wherein R^{43} is H.
6. **(Previously presented)** The compound of claim 1, 78 or 79 wherein either R^{7a} is a moiety other than -OMe or R^{7b} is a moiety other than H.
7. **(Previously Presented)** The compound of claim 6 wherein one of R^{7a} and R^{7b} is - $NR^B C(O)R^A$, $-NR^B C(O)OR^A$, $-NR^B SO_2 R^A$, $-NR^B SO_2 NR^A R^{B'}$ or $-NR^B C(O)NR^A R^{B'}$.
8. **(Original)** The compound of claim 7 in which R^B is H, OH or alkyl.
9. **(Previously presented)** The compound of claim 1, 78 or 79 wherein R^{43} is an aliphatic moiety.
10. **(Previously Presented)** The compound of claim 9 wherein R^{43} is an alkyl moiety.
11. **(Previously presented)** The compound of claim 1, 78 or 79 wherein R^{43} is a hydroxyalkyl moiety.
12. **(Previously Presented)** The compound of claim 9 wherein R^{43} is an alkenyl moiety.
13. **(Previously Presented)** The compound of claim 12 wherein the alkenyl moiety is an allyl group.
14. **(Previously presented)** The compound of claim 1, 78 or 79 wherein R^{43} is an acyl moiety.
15. **(Canceled)**

16. **(Previously Presented)** The compound of claim 14 wherein R^{43} is an acyl moiety of the formula $R^A R^B N\text{-alkyl-C(O)-}$.

17. **(Original)** The compound of claim 2, wherein R^{28} and R^{43} are H, R^{7a} is -OMe, and R^{7b} is H.

18. **(Previously Presented)** The compound of claim 6 wherein n is 2, and R^{28} and R^{43} are H.

19. **(Previously presented)** The compound of claim 1, 78 or 79 wherein n is 2.

20-21. **(Canceled)**

22. **(Previously presented)** The compound of claim 1, 78 or 79 wherein the compound has the formula II in which $-OR^{43}$ is in the S orientation.

23. **(Previously presented)** The compound of claim 1, 78 or 79 wherein the compound has the formula II in which $-OR^{43}$ is in the R orientation.

24-40. **(Canceled)**

41. **(Previously presented)** A composition comprising a compound of claim 1, 78 or 79 and one or more pharmaceutically acceptable carriers, diluents or excipients.

42. **(Previously presented)** A method for producing a compound of claim 1, 78 or 79 which comprises contacting a homologous C28 epimer with a titanium tetraalkoxide reagent under suitable conditions and for a sufficient time to permit epimerization.

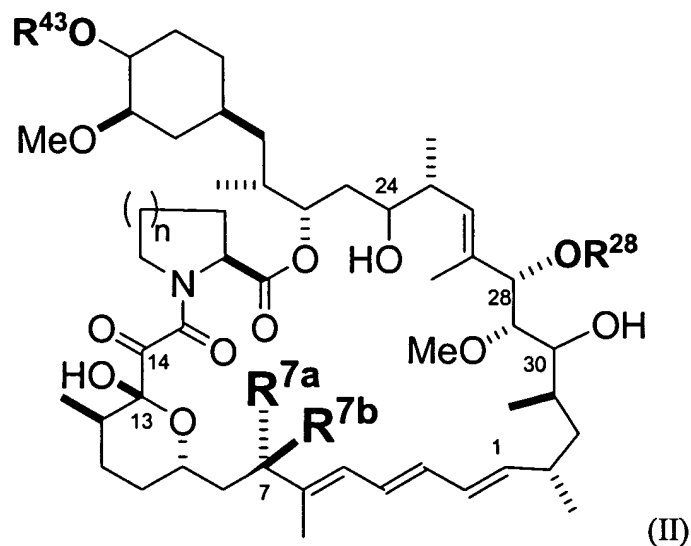
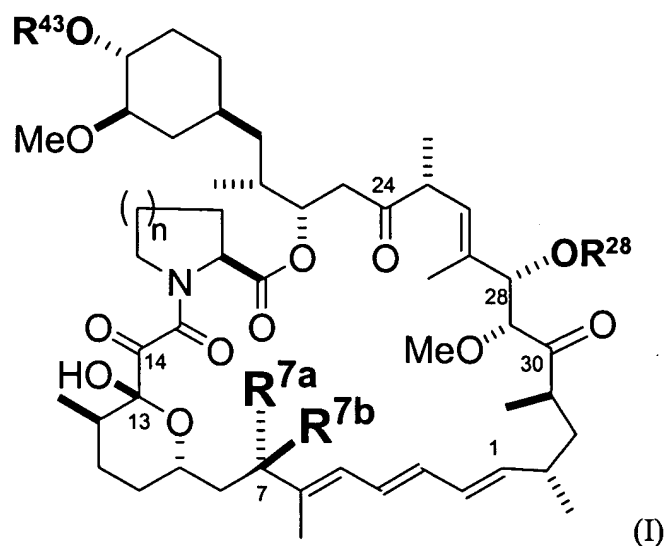
43. **(Original)** The method of claim 42 wherein the titanium tetraalkoxide reagent is titanium tetraisopropoxide.

44. **(Previously Presented)** The method of claim 42 which further comprises recovering the epimerized product.

45. **(Previously presented)** The method of claim 42 wherein the homologous C28 epimer is rapamycin.

46-77. **(Canceled)**

78. **(Currently amended)** A compound of the formula I or II:

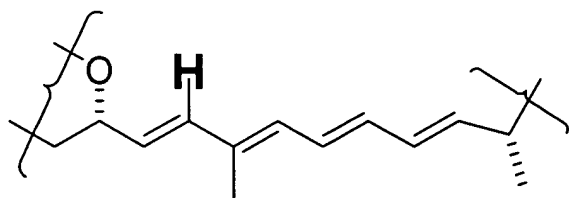


wherein

n is 1 or 2;

R^{28} and R^{43} are independently selected from the group consisting of H and an aliphatic, ~~or acyl, aryl or heteroaryl~~ moiety;

one of R^{7a} and R^{7b} is H and the other is halo, $-R^A$, $-OR^A$, $-SR^A$, $-OC(O)R^A$, $-OC(O)NR^AR^B$, $-NR^AR^B$, $-NR^BC(O)R^A$, $-NR^BC(O)OR^A$, $-NR^BSO_2R^A$, $-NR^BSO_2NR^AR^{B'}$ or $-NR^BC(O)NR^AR^{B'}$; or R^{7a} and R^{7b} taken together, are H in the tetraene moiety:



where R^A is H or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where R^B is H, OH or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where each aliphatic moiety is an independently chosen saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms;

where each heteroaliphatic moiety is an independently chosen 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;

where each aryl moiety is an independently chosen 6-14-membered mono- or polycyclic unsaturated moiety;

where each heteroaryl moiety is an independently chosen 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms;

where each acyl moiety is an independently chosen $-OCR$ group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

wherein each aliphatic, acyl, ~~aryl, heteroaryl~~, heteroaliphatic, aryl, or heteroaryl moiety contains one or more optional substituents selected from the group consisting of $-OH$, $-OR^2$, $-SH$,

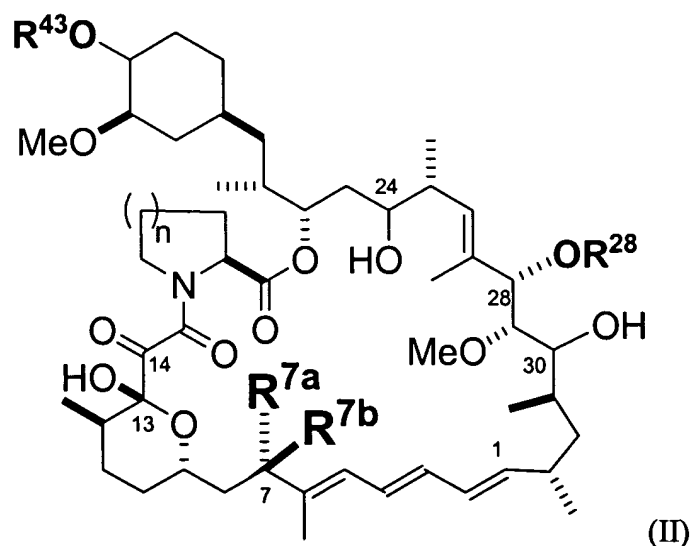
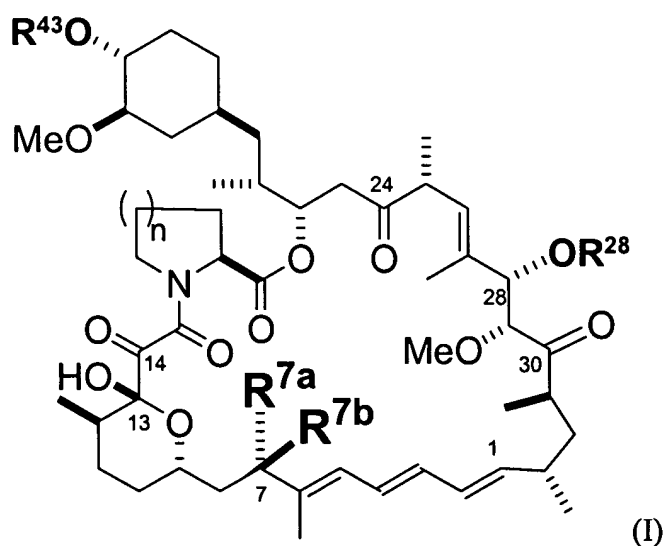
-SR², -CHO, =O, -COOH (or ester, carbamate, urea, oxime or carbonate thereof), -NH₂ (or substituted amine, amide, urea, carbamate or guanidino derivative thereof), halo, trihaloalkyl, cyano, -SO₂-CF₃, -OSO₂F, -OS(O)₂R¹¹, -SO₂-NHR¹¹, -NHSO₂-R¹¹, sulfate, sulfonate, aryl and heteroaryl moieties;

where R² is an aliphatic, heteroaliphatic, aryl, heteroaryl or alkylaryl moiety; and

where R¹¹ is H or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety;

or a pharmaceutically acceptable salt thereof.

79. (Currently amended) A compound of the formula I or II:

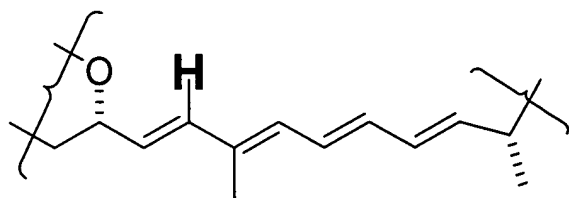


wherein

n is 1 or 2;

R^{28} and R^{43} are independently selected from the group consisting of H and an aliphatic, or acyl, ~~areyl or heteroareyl~~ moiety;

one of R^{7a} and R^{7b} is H and the other is halo, $-R^A$, $-OR^A$, $-SR^A$, $-OC(O)R^A$, $-OC(O)NR^AR^B$, $-NR^AR^B$, $-NR^BC(O)R^A$, $-NR^BC(O)OR^A$, $-NR^BSO_2R^A$, $-NR^BSO_2NR^AR^{B'}$ or $-NR^BC(O)NR^AR^{B'}$; or R^{7a} and R^{7b} taken together, are H in the tetraene moiety:



where R^A is H or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where R^B is H, OH or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where each aliphatic moiety is an independently chosen saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms;

where each heteroaliphatic moiety is an independently chosen 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;

where each aryl moiety is an independently chosen 6-14-membered mono- or polycyclic unsaturated moiety;

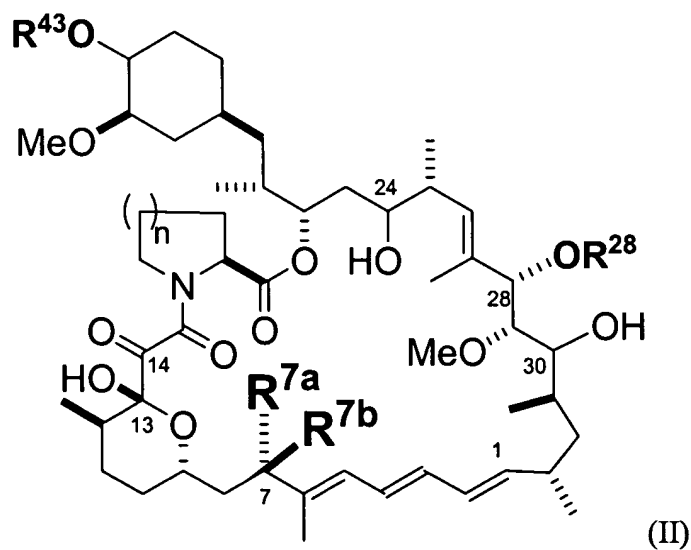
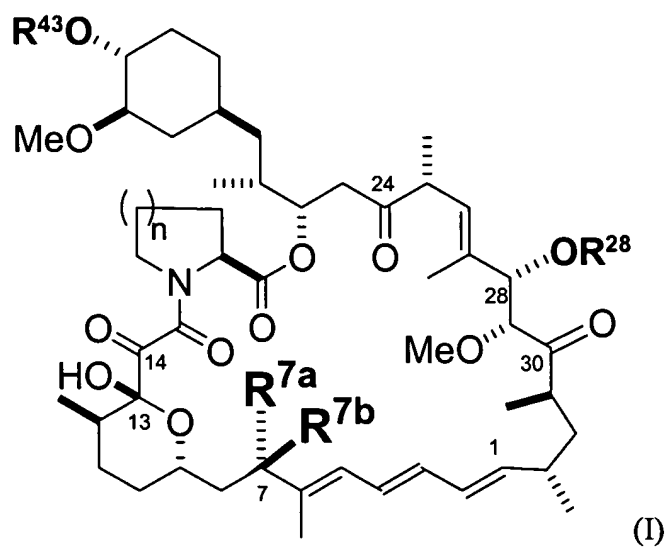
where each heteroaryl moiety is an independently chosen 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms;

where each acyl moiety is an independently chosen $-OCR$ group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

wherein each ~~areyl, heteroareyl~~, aryl or heteroaryl moiety contains one or more optional substituents selected from the group consisting of hydroxy, C1-C8 alkoxy, C1-C8 branched or

straight-chain alkyl, acyloxy, carbamoyl, amino, N-acylamino, nitro, halo, trihalomethyl, cyano, and carboxyl;
or a pharmaceutically acceptable salt thereof.

80. (Currently amended) A compound of the formula I or II:



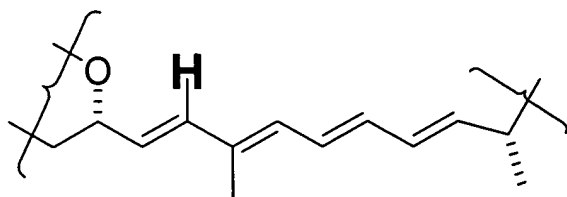
wherein

n is 1 or 2;

R²⁸ is selected from the group consisting of H and an aliphatic, ~~or acyl, aryl or heteroaryl~~ moiety;

R⁴³ is an alkyl, alkenyl or acyl moiety;

one of R^{7a} and R^{7b} is H and the other is halo, -R^A, -OR^A, -SR^A, -OC(O)R^A, -OC(O)NR^AR^B, -NR^AR^B, -NR^BC(O)R^A, -NR^BC(O)OR^A, -NR^BSO₂R^A, -NR^BSO₂NR^AR^{B'} or -NR^BC(O)NR^AR^{B'}; or R^{7a} and R^{7b} taken together, are H in the tetraene moiety:



where R^A is H or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where R^B is H, OH or an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where each aliphatic moiety is an independently chosen saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms;

where each heteroaliphatic moiety is an independently chosen 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;

where each aryl moiety is an independently chosen 6-14-membered mono- or polycyclic unsaturated moiety;

where each heteroaryl moiety is an independently chosen 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms;

where each acyl moiety is an independently chosen -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

wherein each alkyl, alkenyl or acyl moiety contains one or more optional substituents selected from the group consisting of -OH, -OR², -SH, -SR², -CHO, =O, -COOH (or ester, carbamate, urea, oxime or carbonate thereof), -NH₂ (or substituted amine, amide, urea, carbamate or guanidino derivative thereof), halo, trihaloalkyl, cyano, -SO₂-CF₃, -OSO₂F, -OS(O)₂R¹¹, -SO₂-

NHR¹¹, -NHSO₂-R¹¹, sulfate, sulfonate, aryl and heteroaryl moieties;
where R² is an aliphatic, heteroaliphatic, aryl, heteroaryl or alkylaryl moiety; and
where R¹¹ is H or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety;
or a pharmaceutically acceptable salt thereof.

81. **(Previously presented)** 28-epirapamycin or a pharmaceutically acceptable salt thereof.

82. **(Previously presented)** 29-epirapamycin or a pharmaceutically acceptable salt thereof.

83. **(Previously presented)** 28, 29-bis-epirapamycin or a pharmaceutically acceptable salt thereof.

84. **(Currently amended)** A compound having the structure of 28-epirapamycin, 29-epirapamycin or 28, 29-bis-epirapamycin except that the hydroxyl group at position 43 is replaced with OR⁴³ wherein R⁴³ is an aliphatic, or acyl, aryl or heteroaryl moiety;
where an aliphatic moiety is a saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms;
where an acyl moiety is an -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;
where a heteroaliphatic moiety is a 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;
where an aryl moiety is a 6-14-membered mono- or polycyclic unsaturated moiety;
where a heteroaryl moiety is a 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms; and
~~where an acyl moiety is an -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;~~
or a pharmaceutically acceptable salt thereof.

85. **(Currently amended)** A compound having the structure of 28-epirapamycin, 29-epirapamycin or 28, 29-bis-epirapamycin except that the hydroxyl group at position 43 is replaced with OR⁴³ wherein R⁴³ is an aliphatic, or acyl, aryl or heteroaryl moiety;

where an aliphatic moiety is a saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms;

where an acyl moiety is an -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where a heteroaliphatic moiety is a 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;

where an aryl moiety is a 6-14-membered mono- or polycyclic unsaturated moiety;

where a heteroaryl moiety is a 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms;

~~where an acyl moiety is an -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;~~

wherein each aliphatic, or acyl, ~~aryl or heteroaryl~~ moiety contains one or more optional substituents selected from the group consisting of -OH, -OR², -SH, -SR², -CHO, =O, -COOH (or ester, carbamate, urea, oxime or carbonate thereof), -NH₂ (or substituted amine, amide, urea, carbamate or guanidino derivative thereof), halo, trihaloalkyl, cyano, -SO₂-CF₃, -OSO₂F, -OS(O)₂R¹¹, -SO₂-NHR¹¹, -NHSO₂-R¹¹, sulfate, sulfonate, aryl and heteroaryl moieties;

where R² is an aliphatic, heteroaliphatic, aryl, heteroaryl or alkylaryl moiety; and

where R¹¹ is H or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety;

or a pharmaceutically acceptable salt thereof.

86. **(Currently amended)** A compound having the structure of 28-epirapamycin, 29-epirapamycin or 28, 29-bis-epirapamycin except that the hydroxyl group at position 43 is replaced with OR⁴³ wherein R⁴³ is an ~~aliphatic, acyl~~, aryl or heteroaryl moiety;

where an aroyl moiety is an -OCR group where R is an aryl moiety;

where a heteroaroyl moiety is an -OCR group where R is a heteroaryl moiety;

~~where an aliphatic moiety is a saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms;~~

~~where a heteroaliphatic moiety is a 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;~~

where an aryl moiety is a 6-14-membered mono- or polycyclic unsaturated moiety;

where a heteroaryl moiety is a 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms; and
~~where an acyl moiety is an -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;~~

wherein each aroyl or heteroaroyl moiety contains one or more optional substituents selected from the group consisting of hydroxy, C1-C8 alkoxy, C1-C8 branched or straight-chain alkyl, acyloxy, carbamoyl, amino, N-acylamino, nitro, halo, trihalomethyl, cyano, and carboxyl; or a pharmaceutically acceptable salt thereof.

87. **(Currently amended)** The A compound of claim 85 having the structure of 28-
~~epirapamycin, 29-epirapamycin or 28, 29-bis-epirapamycin except that the hydroxyl group at position 43 is replaced with OR⁴³ wherein R⁴³ is an aliphatic, acyl, aroyl or heteroaroyl moiety; where an aliphatic moiety is a saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms; where a heteroaliphatic moiety is a 2-8 membered non-cyclic or 3-10 membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms; where an aryl moiety is a 6-14 membered mono- or polycyclic unsaturated moiety; where a heteroaryl moiety is a 5-6 membered monocyclic or 9-14 membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms; where an acyl moiety is an -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;~~
wherein R⁴³ is a hydroxyalkyl moiety that contains one or more optional substituents selected from the group consisting of -OH, -OR², -SH, -SR², -CHO, -O-, -COOH (or ester, carbamate, urea, oxime or carbonate thereof), -NH₂ (or substituted amine, amide, urea, carbamate or guanidino derivative thereof), halo, trihaloalkyl, cyano, -SO₂-CF₃, -OSO₂F, -OS(O)₂R¹⁺, -SO₂-NHR¹⁺, -NHSO₂-R¹⁺, sulfate, sulfonate, aryl and heteroaryl moieties;
where R² is an aliphatic, heteroaliphatic, aryl, heteroaryl or alkylaryl moiety; and
where R¹⁺ is H or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety;
or a pharmaceutically acceptable salt thereof.

88. **(Currently amended)** A compound having the structure of 28-epirapamycin, 29-epirapamycin or 28, 29-bis-epirapamycin except that the hydroxyl group at position 43 is replaced with OR⁴³ wherein R⁴³ is an ~~aliphatic, acyl, aryl or heteroaryl~~ moiety;

where an acyl moiety is an -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;

where an aliphatic moiety is a saturated or unsaturated, branched or unbranched, cyclic or polycyclic, aliphatic hydrocarbon containing 1-8 contiguous aliphatic carbon atoms;

where a heteroaliphatic moiety is a 2-8-membered non-cyclic or 3-10-membered cyclic aliphatic moiety which contains one or more oxygen, sulfur, nitrogen, phosphorous or silicon atoms;

where an aryl moiety is a 6-14-membered mono- or polycyclic unsaturated moiety;

where a heteroaryl moiety is a 5-6-membered monocyclic or 9-14-membered polycyclic unsaturated moiety which contains one or more oxygen, sulfur or nitrogen atoms;

~~where an acyl moiety is an -OCR group where R is an aliphatic, heteroaliphatic, aryl, or heteroaryl moiety;~~

wherein R⁴³ ~~is an~~ each acyl moiety that contains one or more optional substituents selected from the group consisting of -OH, -OR², -SH, -SR², -CHO, =O, -COOH (or ester, carbamate, urea, oxime or carbonate thereof), -NH₂ (or substituted amine, amide, urea, carbamate or guanidino derivative thereof), halo, trihaloalkyl, cyano, -SO₂-CF₃, -OSO₂F, -OS(O)₂R¹¹, -SO₂-NHR¹¹, -NHSO₂-R¹¹, sulfate, sulfonate, aryl and heteroaryl moieties;

where R² is an aliphatic, heteroaliphatic, aryl, heteroaryl or alkylaryl moiety; and

where R¹¹ is H or an aliphatic, heteroaliphatic, aryl or heteroaryl moiety;

or a pharmaceutically acceptable salt thereof.

89. **(Previously presented)** The compound of claim 1, 78 or 79, wherein the compound has the formula I.

90. **(Previously presented)** The compound of claim 1, 78 or 79, wherein the compound has the formula II.

91. **(New)** The compound of claim 1, 78 or 79, wherein R²⁸ and R⁴³ are independently selected from the group consisting of H and an aliphatic, aryl or heteroaryl moiety.

92. (New) The compound of claim 80, wherein R^{28} is selected from the group consisting of H and an aliphatic, aroyl or heteroaroyl moiety.
93. (New) The compound of claim 84 or 85, wherein R^{43} is an aliphatic, aroyl or heteroaroyl moiety.
94. (New) The compound of claim 88, wherein R^{43} is an aroyl or heteroaroyl moiety.